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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,138	02/13/2002	Darrell R. Anderson	P 0280705 1995-30-0233CP1	7969

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Pillsbury Winthrop LLP
Intellectual Property Group
1600 Tysons Boulevard
McLean, VA 22102

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,138	ANDERSON ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 11/4/04, has been entered.
Claims 1-28 have been canceled.
Claims 29-56 have been added.

Applicant's election traverse of the administration of anti-CD80 / anti-B7.1 antibodies in the treatment of a disease, as it reads on B cell lymphoma is acknowledged.

Given that the current claims are limited to the election of inhibiting or prevent T cell / B cell interactions associated with B cell lymphoma, the previous restriction and species requirements have been rendered moot.

Claims 29-56 are pending and being acted upon as they read on the election invention of administering anti-CD80 / anti-B7.1 antibodies to treat B cell lymphoma.

2. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 29-42, 36, 50 and 55-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A . Claims 29-42: Preventing T cell / B cell interaction associated with B cell lymphoma":

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunotherapeutic regimens can be species- and model-dependent, it is not clear that reliance on the ability of B7-1-specific antibodies to block B7-mediated interactions or treat B cell lymphoma accurately reflects the relative ability of the claimed invention "to prevent T cell / B cell interaction associated with B cell lymphoma" in the context of preventing B cell lymphoma.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has not effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus/insult occur at the same or nearly the same time. Immunosuppression or suppression of tumor / lymphoma growth is much easier to achieve under such controlled conditions than that experienced in the human immunoregulatory diseases such as the B cell lymphoma targeted by the claimed invention.

With respect to "preventing", the skilled artisan does not readily treat nor predict treatment of B cell lymphomas by preventing B cell lymphoma growth by preventing B and T cell interactions.

The histopathology, stage of disease and results of surface marker studies significantly influence the prognosis and response to treatment of lymphomas. In addition, diagnosis requires differentiating the type of lymphoma from other lymphomas, leukemias and other causes of lymphadenopathy. Diagnosis is made by histologic study of excised tissue.

Therefore, the skilled artsian would not predict preventing the occurrence of B cell lymphoma. Rather the skilled artsian treats B cell lymphoma after its presence is diagnosed.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective therapies of preventing the occurrence B cell lymphomas antibodies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods to prevent B cell lymphoma occurrence and growth.

As indicated below, the metes and bounds of the claimed methods are ill-defined and confusing.

Applicant is invited to amend the claims to clear indicate the nature of the claimed methods.

B) Claims 41-42 and 55-56: Combination Therapy with Immunomodulators and Immunosuppressants:

The instant are drawn to the use of immunomodulators (e.g. claims 41 and 55) and immunosuppressants (e.g. claims 42 and 56) in addition to the anti-CD80 antibodies to treat B cell lymphoma.

Given that these immunomodulators and immunosuppressant inhibit immune responses, the skilled artisan would not necessarily predict that inhibiting immune responses would be the best interests of treating a B cell lymphoma patient. The skilled artisan would prefer to maintain the health and immune status of a cancer patient and not to immunosuppress said patient.

As pointed out by Weiner et al. (Expert Opin. Biol. Ther 4: 375-385, 2004), the art still does not have a clear understanding of the mechanism of action responsible for the efficacy of monoclonal antibody therapy of lymphomas (see entire document, including Mechanisms of Action on page 376-377, including page 376, column 2, paragraph 1). This review of monoclonal antibody therapy of lymphoma describes various antibody specificities and mechanisms of actions of treating lymphomas (see entire document).

However, none of the immunomodulators or immunosuppressant recited in the instant claims are described in the context of treating lymphoma.

Further, for example, with respect to anti-LFA-1 (CD11a) and anti-ICAM (CD54) antibodies, Mehta et al. (Cellular Immunology 155: 95 –110, 1994) describe the ability of antibodies to LFA-1 and ICAM-1 to inhibit LAK cell cytotoxicity of B cell lymphomas (see entire document, including the Abstract).

Given that the additional therapeutic agents do not target B cell lymphoma directly and serve to inhibit immune responses that may be responsible for resisting B cell lymphoma or in aiding the treatment of B cell lymphoma, the skilled artisan would not predict inhibiting immune responses in a cancer patient would serve in aiding the treatment of B cell lymphoma in combination with anti-CD80 / anti-B7.1 antibodies, as encompassed by the claimed methods.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective therapies of treating B cell lymphoma with antibodies, including the use of immunosuppressive agents as recited, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods employing combining immunomodulators and/or immunosuppressants in combination with anti-CD80 antibodies to treat B cell lymphoma.

Applicant is invited to provide objective evidence that the specific recited in claim would aid in the treatment of B cell lymphoma.

C) Claims 36 and 50: Deposit of the 7C10 and 16C10 antibodies:

It is apparent that the 7C10 and 16C10 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the appropriate cell line / hybridoma which produces these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Affidavits and declarations, such as those under 37 C.F.R. § 1.131 and 37 C.F.R. § 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

It is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific 7C10 and 16C10 antibodies requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences.

In contrast, it is noted that the recitation of claim 33 requires only the variable regions of said 7C10 and 16C10 antibodies and do not require the entire native 7C10 and 16C10 antibodies.

Therefore, the deposit requirement under 35 USC 112, first paragraph, enablement set forth herein is only directed towards the recitation of the 7C10 and 16C10 antibodies in claims 36 and 50.

5. Claim 29-42 and 55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 29-42 are indefinite in the recitation of "inhibiting or preventing T cell / B cell interactions associated with B cell lymphoma" because the metes and bounds of the methods are ill-defined and indefinite.

For example, it is not clear whether the targeted patient population is a patient with B cell lymphoma or whether the claims read on patient populations other than those with B cell lymphoma.

The claims recite "inhibiting or preventing T cell / B cell interactions associated with B cell lymphoma". However, it is unclear whether the claims necessarily read on a patient with B cell lymphoma and one is inhibiting or preventing T cell / B cell interactions associated with the B cell lymphoma per se, or whether the claims read on inhibiting or preventing T cell / B cell interactions which are associated with B cell lymphoma but the claims methods do not require that the anti-CD80 antibodies need to administered to a patient with B cell lymphoma.

Applicant is invited to consider amending the claims to simply read on "treating B cell lymphoma" or clearly reciting the B cell lymphoma targeted patient population as it reads on the elected invention.

B) Claims 41 and 55 are indefinite in that the proper antecedent basis for "fragment thereof" is unclear. For example, does "or fragment thereof" modify only "anti-CD28 antibodies" or modifies "IL-17, IL-10, CTLA4-Ig and/or soluble CTLA-4"

C) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

6. The following objections are noted.

A) Claims 42 and 56 are objected to as they claims should recite anti-TNFα antibody, anti-CD54 antibody, anti-CD11 antibody, etc. rather than simply "anti-TNFα, anti-CD54, anti-CD11", as currently recited, to clearly indicate that these molecules are antibodies.

B) Claims 29-42 and 50-51are objected to in that the recitation of "CD80 antigen" (see claim 29, lines 5-6; claims 36-37, 50-51) should be amended to simply recite CD80 for clarity and consistency with the rest of the claim 29 as well as the pending claims.

7. Given the prosecution of related applications with respect to the claimed antibody specificity as it reads on anti-CD80 / anti-B7.1 antibodies that inhibit the binding of B cell and T cells via the CD80/CD28 pathway without inhibiting the binding of CD80 antigen to CTLA-4 appears free of the prior art.

8. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 29-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-26, 32 and 37 of copending application USSN 09/758,173. Although the conflicting claims are not identical, they are not patentably distinct from both sets of claims appear to drawn to the same or nearly the same methods of treating B cell lymphoma with the same or nearly the same CD80-specific antibodies that inhibit the binding of B cells and T cells via the CD80/CD28 pathway without inhibiting the binding of CD80 to CTLA-4. The instant recitation of "inhibiting or preventing T cell / B cell interactions associated with B cell lymphoma" is one of mode of action of the anti-CD80 antibodies. The claimed inventions of "treating patients with B cell lymphoma with the claimed CD80-specific antibodies" of both applications anticipate one another.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 29-56 are directed to an invention not patentably distinct from claims 23-26, 32 and 37 of commonly assigned USSN 09/758,173 for the reasons above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
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